DOI:
10.1016/j.conb.2018.05.003

Document Version
Peer reviewed version

Contextual signals in visual cortex

Adil G. Khan[1], Sonja B. Hofer[2]

1. Centre for Developmental Neurobiology, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
2. Sainsbury Wellcome Centre for Neural Circuits and Behaviour, University College London, London, UK

Adil G. Khan: khan.adil@kcl.ac.uk; Sonja B. Hofer: s.hofer@ucl.ac.uk

Correspondence to: S.B.H. s.hofer@ucl.ac.uk

Highlights

- Visual processing can be strongly influenced by intentions, expectations or actions
- Recent work has uncovered novel top-down and modulatory circuits influencing vision
- Understanding these circuits gives insights into cortical function and flexibility

Abstract

Vision is an active process. What we perceive strongly depends on our actions, intentions and expectations. During visual processing, these internal signals therefore need to be integrated with the visual information from the retina. The mechanisms of how this is achieved by the visual system are still poorly understood. Advances in recording and manipulating neuronal activity in specific cell types and axonal projections together with tools for circuit tracing are beginning to shed light on the neuronal circuit mechanisms of how internal, contextual signals shape sensory representations. Here we review recent work, primarily in mice, that has advanced our understanding of these processes, focusing on contextual signals related to locomotion, behavioural relevance and predictions.

Introduction

The classical model of information processing in the brain is based on a hierarchical organization of feedforward connections from one brain region to the next. In the visual system, information from the retina is relayed via the dorsolateral geniculate nucleus (dLGN) in the thalamus to the primary visual cortex (V1), and from there through a hierarchy of increasingly higher-order cortical areas [1]. In this hierarchical model, visual cortex neurons are mainly seen as feature detectors that signal the presence of a specific visual stimulus in the environment, while feedback connections have a minor, modulatory influence. This view remains a cornerstone of our understanding of visual processing.

However, we understand only a small fraction of activity even in V1 [2], and many aspects of visual responses cannot be predicted by feedforward models [3]. This is not surprising given that less than 10 % of synapses received by cortical neurons stem from feedforward projections [4]. It is now well established that in behaving animals, visual responses can be strongly influenced by contextual cues, such as visual scene context, attention, self-movement, task requirements, spatial location and expectations [5–11]. Visual processing therefore is likely to be an active process, involving internal models of the world and dependent on the behavioural and perceptual needs of the animal.

At the circuit level, contextual influences are thought to be conveyed via top-down projections from higher brain areas, intra-areal horizontal connections or neuromodulatory inputs. However, circuit mechanisms of contextual modulation have often been difficult to identify, and hence our understanding of the sources of specific contextual signals and how they are integrated with feedforward sensory information is still very limited. Advances in genetic tools for labelling specific cell types and circuits, and monitoring or manipulating their activity in behaving rodents are beginning to advance our understanding of how contextual and visual signals are combined during active vision. This review focuses on a few specific areas which have witnessed particularly interesting developments in recent years: contextual signals related to locomotion, behavioural relevance and predictions.

Effects of locomotion on visual cortex activity

Behavioural state has a strong influence on cortical processing [12,13]. For instance, visual responses in V1 are stronger, more reliable, and less correlated when mice walk or run compared to when they are quietly resting [14–16]. These effects show similarities to modulation of responses by arousal or attention [17–20,9]. Locomotion-related response modulation in visual cortex is thought to be at least partly conveyed by cholinergic input from the basal forebrain, which is activated by projections from the mesencephalic locomotor region during running [21,22] (Figure 1). The cholinergic signals have been shown to strongly act on vasoactive intestinal peptide (VIP) expressing inhibitory interneurons [21]. These inhibit somatostatin (SOM) expressing interneurons, which can lead to disinhibition and thus increased activity of excitatory pyramidal neurons. This disinhibitory motif involving VIP and SOM cells was also found in other cortical areas [23–25] and could provide a more general

mechanism for state-dependent gain modulation [26]. However, other studies found that SOM cells were activated rather than suppressed by locomotion when animals were exposed to light or visual stimuli [27–29]. These seemingly disparate findings could be reconciled by a cortical circuit model that included interactions between multiple inhibitory cell types [30]. The opposite sign of SOM cell responses during locomotion in different visual contexts emerges from the dynamics of the model due to the change in input drive in the presence or absence of visual input.

Neuromodulation by cholinergic and noradrenergic signalling [19,21,27] likely contributes to locomotion-related activity changes in cortex, probably due to increased arousal during locomotion [22] (but see [31]). However, some locomotion-related signals in visual cortex are inconsistent with unspecific gain modulation, but instead provide specific information about self-motion. Pyramidal cells in V1 are active during running in the dark and their firing is modulated by running speed [16,29,32,33]. These motor signals could be inherited from the visual thalamus where locomotor-related activity has been observed both in the dLGN as well as in the higher-order pulvinar complex [16,34]. In addition, anterior cingulate and neighbouring secondary motor cortex (ACC/M2) convey strong motor signals to V1. These projections specifically activate running-modulated V1 cells and silencing ACC/M2 decreases locomotion-triggered V1 responses [35]. Such motor signals could represent an efference copy that informs visual processing of the animal's self-motion (see below).

Locomotion has further effects on visual responses, including decreased surround suppression, and increased spatial sensitivity in visual cortex [16,36,37]. Together, the described changes might adapt visual processing to the needs of an animal moving through its environment.

Learning the behavioural relevance of visual stimuli

When a sensory stimulus becomes behaviourally relevant, its representation in sensory cortical networks is enhanced, including expanded cortical representations, increased or more reliable and selective responses, changes in stimulus tuning and decreased response correlations. Many of these changes are already visible at the earliest stages of cortical processing. Repetitive practice in a perceptual task can further improve sensory responses. These can facilitate the read-out and interpretation of sensory signals relevant to the task to better inform behavioural decisions, and may even directly couple to behavioural output through projections to the striatum [38]. Previous reviews have comprehensively covered the effects of behavioural stimulus relevance and learning on visual cortical areas, focusing on various contributing factors, including perceptual learning, different forms of attention, reward expectation, and flexible circuit adaptations to the requirements of a task [8,9,39–41]. Here we focus on recent studies that have started to elucidate the circuit mechanisms of learning-related changes in visual circuits as well as the role of top-town signals from higher brain areas.

Two-photon imaging of genetically-encoded calcium indicators enables tracking the neuronal responses of identified neurons over the time-course of learning [42]. Using this method, Poort et al found that when mice learned a visual discrimination task, V1 population responses

become increasingly better at discriminating the task-relevant stimuli. This improvement in stimulus encoding resulted from an increase in the number of selective neurons and greater day-to-day stability of selective responses [43]. Visual response selectivity decreased when trained mice engaged in a non-visual task, but was still higher than before learning, even under anaesthesia. This suggests that learning the behavioural relevance of sensory stimuli engages task-dependent top-down influences which act in concert with more permanent circuit modifications in V1 [43,44]. Local circuit changes in V1 are associated with increased stimulus selectivity of parvalbumin-expressing interneurons [45], which thereby provide more selective inhibition during processing of behaviourally relevant stimuli.

Top-down inputs potentially contribute to learning-induced neural response changes in several ways. Learning can change the strength and/or nature of signals conveyed to visual cortex from specific higher brain areas. For instance, axonal projections in V1 from retrosplenial cortex increase their activity as mice learn to react to a visual input in order to escape an aversive stimulus, thereby altering visual responses of layer 2/3 cells [46]. Anterior cingulate cortex (ACC) is another major source of long-range input to V1 [47], and has been shown to convey task-dependent, contextual signals during visually-guided behaviour [10,35]. Moreover, optogenetic activation of ACC enhances V1 responses and improves behavioural performance in a visual discrimination task [47]. Changes in top-down influences also likely underlie the emergence of stimulus anticipation and behavioural-choice related signals in subsets of V1 neurons during visual discrimination learning [43]. Interestingly, these signals develop preferentially in cells with stronger responses to the rewarded compared to the non-rewarded stimulus, suggesting that during learning top-down signals selectively target subsets of functionally defined cells. Intriguingly, cortical top-down signals may not always exert their effects directly, but might also act through the thalamus: a recent study indicates that prefrontal cortex projections to the thalamic reticular nucleus modulate the gain of visual cortex responses during cross-modal attention [48].

Top-down signals may also enable or gate learning-related plasticity in visual circuits. Top-down projections often densely innervate layer 1, where they can depolarize apical dendrites of pyramidal neurons, potentially facilitating the association of other long-range or local inputs with bottom-up information (Figure 2). This has been shown to be the case in mouse somatosensory cortex (S1), where higher order thalamic inputs evoke dendritic plateau potentials which are crucial for whisker-evoked LTP [49]. Lesions of the pulvinar (the higher-order visual thalamic nucleus) also lead to visual learning impairments [50] suggesting that similar mechanisms may exist in the visual system. Enabling plasticity in the dendrites of pyramidal cells might involve the release of inhibition from SOM interneurons, which have been suggested to regulate learning-related changes in V1 and S1 [46,51,45]. The notion that learning can be gated by top-down signals has been formalized in a biologically plausible model of reinforcement learning [52,41]. In this model, synaptic tagging mediated by top-down signals is followed by a global reinforcement signal which results in subsequent strengthening of the tagged synapses. A likely candidate for the reinforcement signal is the neuromodulator acetylcholine, which signals behavioural outcome or salience [53], modifies top-down

processing [54] and induces reward-related changes in V1 activity [55,56]. In addition, after learning, general effects of task engagement or arousal on neuronal responses might also be caused by cholinergic or noradrenergic neuromodulation [19,27,57,58].

Predictive coding

Through experience and learning, the brain builds internal models of the world around us. These models continuously generate predictions about our environment which help to interpret sensory information and thus shape perception, as apparent in various optical illusions which play with our expectations about a visual stimulus [59] (Figure 3a,b). Hence, visual processing is strongly influenced by internal models and expectations. The theoretical framework of predictive coding [60–62] postulates that stimulus representation in sensory cortical areas is mainly constructed from top-down prediction signals conveyed by higher-order brain regions, while feed-forward information carries a so-called prediction error, the difference between what is predicted and the actual sensory input (Figure 3c). This error or mismatch signal is then used to update the model prediction. According to this theory, in a sensory cortical area, one subset of neurons encodes the current 'best guess' of the stimulus while another subset is dedicated to encoding how the actual sensory input deviates from the predictions. The relative balance of top-down predictions and external drive may be flexible, for instance, depending on the fidelity of sensory input, certainty of a prior expectation, or other behavioural demands.

However, until recently direct neurophysiological evidence for this framework in cortical processing has been very scarce (but see e.g.[63–67]). A series of recent studies have provided strong evidence for predictive coding in neocortical circuits, including top-down prediction signals, a circuit for cancelling out predictable sensory input, and prediction error signals in an early sensory region. These studies mostly utilized locomotion of head-fixed mice on a spherical treadmill in a virtual reality (VR) environment. Self-motion causes highly predictable optic flow, and in a VR environment this visual feedback signal can be manipulated and uncoupled from the locomotion of the animal to create visual input that deviates from what would be expected from the animal's movement. Keller and colleagues found that a subset of neurons in V1 selectively responded to such mismatches between the predicted and actual optic flow [68]. These error signals were specific to particular locations in visual space, resulting in mismatch receptive fields [69]. Importantly, these mismatch responses only develop with normal visuo-motor experience [70] and are therefore consistent with prediction error signals, which require top-down predictions from learnt, internal models. A local circuit mechanism in V1 may underlie such error signals resulting from optic flow that is absent or slower than expected when animals are running: subsets of V1 neurons receive excitatory drive from an efference copy input carrying information about the animal's running speed, and are suppressed by optic flow via SOM cell-mediated inhibition [70] (Figure 3c). In the absence of optic flow, SOM cells are less active, inhibition is released, and the continuing optic flow prediction signal therefore induces pyramidal cell firing giving rise to mismatch responses [70].

Where does the prediction signal arise? In a recent study, Leinweber et al. characterized motor-related input to mouse V1 from area ACC/M2 that can provide the prediction of self-generated visual feedback. As expected from the predictive coding framework, suppressing ACC/M2 input decreased visuomotor mismatch responses in V1 [35]. Moreover, inputs from ACC/M2

to V1 - as assessed by calcium imaging in axonal boutons - differed depending on the nature of visuo-motor coupling: motor-related responses changed when mice were trained in a 2D VR environment with left-right inverted optic flow, such that the ACC/M2 signal reflected the newly learnt consequences of self-motion. Interestingly, this change occurred despite the fact that mice experienced this reversed world for only an hour each day, and responses reverted when trained mice ran without optic flow feedback or with optic flow uncoupled from their movements. This top-down signal is thus highly dependent on visuomotor experience, and presumably is able to flexibly update predictions about incoming sensory information depending on the context and learned internal models of visuomotor coupling.

Visuomotor mismatch signals have also been found in the pulvinar, a higher-order visual area in the thalamus which is thought to be important for visual attention and coordination of information flow between cortical areas [71,34]. Pulvinar is highly interconnected with all levels of the cortical visual processing hierarchy, and is well situated to balance top-down and bottom-up influences. For instance, error-related signals from pulvinar to visual cortex could control the gain of cortical error responses, thus increasing the saliency of novel or unexpected visual signals [34,72].

Evidence that stimulus expectation strongly influences visual processing is not restricted to sensorimotor interactions. As mice learn to navigate a VR corridor, some neurons in visual cortex develop predictive responses to upcoming visual stimuli based on their spatial location [43,10], and omission of expected visual stimuli or landmarks evokes strong activity in V1, potentially reflecting prediction errors [10,73].

Conclusions and Outlook

It remains to be shown to what degree top-down predictions and other contextual signals influence or even dominate visual cortex responses and sensory representations in general. However, the reviewed studies, together with extensive previous literature, emphasize that sensory processing is highly dynamic, allowing animals to flexibly access and process sensory information according to their current perceptual and behavioural demands. The strong influence of contextual information on sensory representations, even at the early stages of sensory cortical processing, is not specific to rodents, but has also been demonstrated in primates and humans [66,8,74–76,41]. However, contextual influences may vary substantially across species depending on ethological relevance. For instance, eye-movement related signals in visual cortex of the afoveate mouse [77] are only partially reminiscent of those observed in primates [78].

This brief review highlights research that has begun dissecting the circuit mechanisms of integration of specific top-down signals in visual cortex. However, under natural conditions in the behaving animal, individual contextual signals will rarely occur in isolation, but instead contribute to a rich barrage of contextual inputs from various sources. Future work will have to elucidate how these diverse contexts are combined to inform sensory processing and perception. This will require the refinement of existing theories (such as predictive coding) along with further identification of the underlying circuit mechanisms, which likely involve complex interactions between long-range projections with different inhibitory and excitatory

cell types. To complicate matters further, the role of a given cell class may itself be flexible: VIP cells have been shown to both disinhibit or inhibit principal pyramidal neurons in different contexts [21,26,47,79]. Moreover, different cortical layers might play distinct, complementary roles for the integration of top down and bottom up information [61,80].

Finally, our knowledge of the sources of different contextual signals is still very limited. Top-down signals are typically attributed to projections from higher cortical areas [81,8,82]. However, recent work has provided intriguing evidence for the importance of non-cortical structures such as the superior colliculus, the cerebellum, and the basal ganglia in providing contextual information about sensorimotor and internal variables [83–85]. Signals from subcortical structures converge on diverse thalamic nuclei, which, rather than just relaying information, likely integrate subcortical signals and dynamically interact with cortical pathways [48,34,86,87]. We suggest that visual perception, rather than relying on the simple summation of feedforward and top-down signals from different brain areas, might arise from complex, reverberating cortio-cortical and cortico-subcortical loops. Future studies will be able to prove or disprove this idea and shed further light on the mechanism of visual perception.

Acknowledgments

We thank Thomas Mrsic-Flogel for comments and feedback on this manuscript. This work was supported by the European Research Council (SBH, HigherVision 337797, and an Ambizione grant from the Swiss National Science Foundation (AGK).

Competing interests

The authors declare no competing financial or non-financial interests

References:

1. Van Essen DC: **Visual areas of the mammalian cerebral cortex**. *Annu Rev Neurosci* 1979, **2**:227–263.
2. Olshausen BA, Field DJ: **How close are we to understanding v1?** *Neural Comput* 2005, **17**:1665–1699.
3. Carandini M, Demb JB, Mante V, Tolhurst DJ, Dan Y, Olshausen BA, Gallant JL, Rust NC: **Do we know what the early visual system does?** *J Neurosci Off J Soc Neurosci* 2005, **25**:10577–10597.
4. Binzegger T, Douglas RJ, Martin KA: **A quantitative map of the circuit of cat primary visual cortex**. *JNeurosci* 2004, **24**:8441–8453.
5. Albright TD, Stoner GR: **Contextual influences on visual processing**. *AnnuRevNeurosci* 2002, **25**:339–379.
6. Gilbert CD, Sigman M: **Brain States: Top-Down Influences in Sensory Processing**. *Neuron* 2007, **54**:677–696.
7. Wurtz RH, McAlonan K, Cavanaugh J, Berman RA: **THALAMIC PATHWAYS FOR ACTIVE VISION**. *Trends Cogn Sci* 2011, **15**:177–184.
8. Gilbert CD, Li W: **Top-down influences on visual processing**. *Nat Rev Neurosci* 2013, **14**.
9. Maunsell JHR: **Neuronal Mechanisms of Visual Attention**. *Annu Rev Vis Sci* 2015, **1**:373–391.
10. Fiser A, Mahringer D, Oyibo HK, Petersen AV, Leinweber M, Keller GB: **Experience-dependent spatial expectations in mouse visual cortex**. *Nat Neurosci* 2016, **19**:1658–1664.

* As mice become familiar with running through a virtual corridor, predictive activity emerges in V1 and anterior cingulate cortex projections to V1, anticipating the appearance of landmarks. Omission of landmarks evokes strong activity in V1, potentially reflecting prediction errors.

11. Angelucci A, Bijanzadeh M, Nurminen L, Federer F, Merlin S, Bressloff PC: **Circuits and Mechanisms for Surround Modulation in Visual Cortex**. *Annu Rev Neurosci* 2017, **40**:425–451.
12. Lee S-H, Dan Y: **Neuromodulation of Brain States**. *Neuron* 2012, **76**:209–222.
13. Poulet JF, Petersen CC: **Internal brain state regulates membrane potential synchrony in barrel cortex of behaving mice**. *Nature* 2008, **454**:881–885.
14. Niell CM, Stryker MP: **Modulation of visual responses by behavioral state in mouse visual cortex**. *Neuron* 2010, **65**:472–479.
15. Bennett C, Arroyo S, Hestrin S: **Subthreshold Mechanisms Underlying State-Dependent Modulation of Visual Responses**. *Neuron* 2013, **80**:350–357.
16. Erisken S, Vaiceliunaite A, Jurjut O, Fiorini M, Katzner S, Busse L: **Effects of locomotion extend throughout the mouse early visual system**. *Curr Biol CB* 2014, **24**:2899–2907.
17. Reynolds JH, Chelazzi L: **Attentional modulation of visual processing**. *AnnuRevNeurosci* 2004, **27**:611–647.
18. Harris KD, Thiele A: **Cortical state and attention**. *Nat Rev Neurosci* 2011, **12**:509–523.
19. Pinto L, Goard MJ, Estandian D, Xu M, Kwan AC, Lee S-H, Harrison TC, Feng G, Dan Y: **Fast modulation of visual perception by basal forebrain cholinergic neurons**. *Nat Neurosci* 2013, **16**:1857–1863.
20. Reimer J, Froudarakis E, Cadwell CR, Yatsenko D, Denfield GH, Tolias AS: **Pupil fluctuations track fast switching of cortical states during quiet wakefulness**. *Neuron* 2014, **84**:355–362.

21. Fu Y, Tucciarone JM, Espinosa JS, Sheng N, Darcy DP, Nicoll RA, Huang ZJ, Stryker MP: **A Cortical Circuit for Gain Control by Behavioral State**. *Cell* 2014, **156**:1139–1152.

22. Lee AM, Hoy JL, Bonci A, Wilbrecht L, Stryker MP, Niell CM: **Identification of a brainstem circuit regulating visual cortical state in parallel with locomotion**. *Neuron* 2014, **83**:455–466.

23. Lee S, Kruglikov I, Huang ZJ, Fishell G, Rudy B: **A disinhibitory circuit mediates motor integration in the somatosensory cortex**. *Nat Neurosci* 2013, **16**:1662–1670.

238 * This study indicates that the effects of locomotion on V1 responses are at least partly conveyed by
239 projections from the mesencephalic locomotor regions to the basal forebrain.

24. Pfeffer CK, Xue M, He M, Huang ZJ, Scanziani M: **Inhibition of inhibition in visual cortex: the logic of connections between molecularly distinct interneurons**. *Nat Neurosci* 2013, **16**:1068–1076.

25. Pi H-J, Hangya B, Kvitsiani D, Sanders JI, Huang ZJ, Kepecs A: **Cortical interneurons that specialize in disinhibitory control**. *Nature* 2013, **503**:521–524.

26. Hangya B, Pi H-J, Kvitsiani D, Ranade SP, Kepecs A: **From circuit motifs to computations: mapping the behavioral repertoire of cortical interneurons**. *Curr Opin Neurobiol* 2014, **26**:117–124.

27. Polack P-O, Friedman J, Golshani P: **Cellular mechanisms of brain state-dependent gain modulation in visual cortex**. *Nat Neurosci* 2013, **16**:1331–1339.

28. Dipoppa M, Ranson A, Krumin M, Pachitariu M, Carandini M, Harris KD: **Vision and locomotion shape the interactions between neuron types in mouse visual cortex**. *bioRxiv* 2016, doi:10.1101/058396.

29. Pakan JM, Lowe SC, Dylda E, Keemink SW, Currie SP, Coutts CA, Rochefort NL: **Behavioral-state modulation of inhibition is context-dependent and cell type specific in mouse visual cortex**. *eLife* 2016, **5**:e14985.

30. Garcia del Molino LC, Yang GR, Mejias JF, Wang X-J: **Paradoxical response reversal of top-down modulation in cortical circuits with three interneuron types**. *eLife* 2017, **6**.

240 * This study presents a cortical circuit model that can explain the findings that SOM cells are either
241 activated or inhibited by running, depending on the presence or absence of visual stimuli. This model
242 relies on the interaction of multiple classes of interneurons with non-linear responses to input.

31. Vinck M, Batista-Brito R, Knoblich U, Cardin JA: **Arousal and locomotion make distinct contributions to cortical activity patterns and visual encoding**. *Neuron* 2015, **86**:740–754.

32. Keller GB, Bonhoeffer T, Hübener M: **Sensorimotor mismatch signals in primary visual cortex of the behaving mouse**. *Neuron* 2012, **74**:809–815.

33. Saleem AB, Ayaz A, Jeffery KJ, Harris KD, Carandini M: **Integration of visual motion and locomotion in mouse visual cortex**. *Nat Neurosci* 2013, **16**:1864.

34. Roth MM, Dahmen JC, Muir DR, Imhof F, Martini FJ, Hofer SB: **Thalamic nuclei convey diverse contextual information to layer 1 of visual cortex**. *Nat Neurosci* 2016, **19**:299–307.

243 * Using two-photon calcium imaging of thalamic projections in V1, this study finds that the lateral
244 posterior nucleus in the thalamus, the mouse homologue of the pulvinar, conveys diverse contextual
245 information to V1, including visuomotor mismatch signals.

35. Leinweber M, Ward DR, Sobczak JM, Attinger A, Keller GB: **A Sensorimotor Circuit in Mouse Cortex for Visual Flow Predictions**. *Neuron* 2017, **95**:1420–1432.e5.

** This study identifies a top-down projection to V1 from anterior cingulate and secondary motor cortex that might convey a prediction of visual flow based on motor output, consistent with the predictive coding framework. This projection carries locomotion-related signals to V1, and when visuo-motor coupling is changed, this signal reflects the newly learnt sensory consequences of self-movement.

36. Ayaz A, Saleem AB, Schölvinck ML, Carandini M: **Locomotion Controls Spatial Integration in Mouse Visual Cortex**. *Curr Biol* 2013, **23**:890–894.

37. Mineault PJ, Tring E, Trachtenberg JT, Ringach DL: **Enhanced Spatial Resolution During Locomotion and Heightened Attention in Mouse Primary Visual Cortex**. *J Neurosci* 2016, **36**:6382–6392.

38. Znamenskiy P, Zador AM: **Corticostriatal neurons in auditory cortex drive decisions during auditory discrimination**. *Nature* 2013, **497**:482–485.

39. Gilbert CD, Li W, Piech V: **Perceptual learning and adult cortical plasticity**. *J Physiol* 2009, **587**:2743–2751.

40. Karmarkar UR, Dan Y: **Experience-Dependent Plasticity in Adult Visual Cortex**. *Neuron* 2006, **52**:577–585.

41. Roelfsema PR, Holtmaat A: **Control of synaptic plasticity in deep cortical networks**. *Nat Rev Neurosci* 2018, **19**:166–180.

42. Huber D, Gutnisky DA, Peron S, O'Connor DH, Wiegert JS, Tian L, Oertner TG, Looger LL, Svoboda K: **Multiple dynamic representations in the motor cortex during sensorimotor learning**. *Nature* 2012, **484**:473–478.

43. Poort J, Khan AG, Pachitariu M, Nemri A, Orsolic I, Krupic J, Bauza M, Sahani M, Keller GB, Mrsic-Flogel TD, et al.: **Learning Enhances Sensory and Multiple Non-sensory Representations in Primary Visual Cortex**. *Neuron* 2015, **86**:1478–1490.

** As mice learn a discrimination task in which they attribute behavioural value to specific visual stimuli, anticipatory and choice related signals emerge in V1. These signals develop in concert with an improvement in stimulus discriminability within the same circuit. Responses to task-relevant stimuli are less selective when mice are engaged in a non-visual task, indicating that task-dependent top-down signals contribute to learning-related changes.

44. Chen JL, Margolis DJ, Stankov A, Sumanovski LT, Schneider BL, Helmchen F: **Pathway-specific reorganization of projection neurons in somatosensory cortex during learning**. *Nat Neurosci* 2015, **18**:1101–1108.

45. Khan AG, Poort J, Chadwick A, Blot A, Sahani M, Mrsic-Flogel TD, Hofer SB: **Distinct learning-induced changes in stimulus selectivity and interactions of GABAergic interneuron classes in visual cortex**. *Nat Neurosci* 2018, **In Press**.

* This study measures neuronal responses of excitatory and three classes of inhibitory neurons during learning, and finds that PV interneurons increase their stimulus selectivity, and functional interactions between pyramidal and PV cells reorganize, leading to stimulus-selective pyramidal-PV ensembles. Moreover, the results of this study indicate that SOM cells gate the learning-induced selectivity increase in pyramidal cells.

46. Makino H, Komiyama T: **Learning enhances the relative impact of top-down processing in the visual cortex**. *Nat Neurosci* 2015, **18**:1116–1122.

* Learning a visually-guided task leads to increased top-down drive from retrosplenial cortex, affecting layer 2/3 cells in V1 which show suppressed visual responses and develop a ramp-up response profile preceding an aversive stimulus.

47. Zhang S, Xu M, Kamigaki T, Do JPH, Chang W-C, Jenvay S, Miyamichi K, Luo L, Dan Y: **Long-range and local circuits for top-down modulation of visual cortex processing**. *Science* 2014, **345**:660–665.

48. Wimmer RD, Schmitt LI, Davidson TJ, Nakajima M, Deisseroth K, Halassa MM: **Thalamic control of sensory selection in divided attention**. *Nature* 2015, **526**:705–709.

* Prefrontal cortex can influence the gain of visual responses through the thalamic reticular nucleus to suit attentional demands.

49. Gambino F, Pagès S, Kehayas V, Baptista D, Tatti R, Carleton A, Holtmaat A: **Sensory-evoked LTP driven by dendritic plateau potentials *in vivo***. *Nature* 2014, **515**:116–119.

** This study shows that sensory-evoked LTP in the somatosensory cortex can occur without the post-synaptic cell spiking. Instead plasticity is enabled by dendritic NMDA mediated plateau potentials driven by projections from higher order thalamus.

50. Chalupa LM, Coyle RS, Lindsley DB: **Effect of pulvinar lesions on visual pattern discrimination in monkeys**. *J Neurophysiol* 1976, **39**:354–369.

51. Williams LE, Holtmaat A: **Higher-order thalamocortical inputs gate synaptic long-term potentiation via disinhibiton**. *bioRxiv* 2018, doi:10.1101/281477.

52. Rombouts JO, Bohte SM, Roelfsema PR: **How Attention Can Create Synaptic Tags for the Learning of Working Memories in Sequential Tasks**. *PLOS Comput Biol* 2015, **11**:e1004060.

53. Hangya B, Ranade SP, Lorenc M, Kepecs A: **Central Cholinergic Neurons Are Rapidly Recruited by Reinforcement Feedback**. *Cell* 2015, **162**:1155–1168.

54. Pafundo DE, Nicholas MA, Zhang R, Kuhlman SJ: **Top-Down-Mediated Facilitation in the Visual Cortex Is Gated by Subcortical Neuromodulation**. *J Neurosci* 2016, **36**:2904–2914.

55. Chubykin AA, Roach EB, Bear MF, Shuler MGH: **A Cholinergic Mechanism for Reward Timing within Primary Visual Cortex**. *Neuron* 2013, **77**:723–735.

56. Liu C-H, Coleman JE, Davoudi H, Zhang K, Hussain Shuler MG: **Selective activation of a putative reinforcement signal conditions cued interval timing in primary visual cortex**. *Curr Biol CB* 2015, **25**:1551–1561.

57. McGinley MJ, David SV, McCormick DA: **Cortical Membrane Potential Signature of Optimal States for Sensory Signal Detection**. *Neuron* 2015, **87**:179–192.

58. Kuchibhotla KV, Gill JV, Lindsay GW, Papadoyannis ES, Field RE, Sten TAH, Miller KD, Froemke RC: **Parallel processing by cortical inhibition enables context-dependent behavior**. *Nat Neurosci* 2017, **20**:62–71.

59. Weiss Y, Simoncelli EP, Adelson EH: **Motion illusions as optimal percepts**. *Nat Neurosci* 2002, **5**:598–604.

60. Rao RP, Ballard DH: **Predictive coding in the visual cortex: a functional interpretation of some extra-classical receptive-field effects**. *NatNeurosci* 1999, **2**:79–87.

61. Friston K: **A theory of cortical responses**. *PhilosTransRSocLond B BiolSci* 2005, **360**:815–836.

62. Clark A: **Whatever next? Predictive brains, situated agents, and the future of cognitive science**. *Behav Brain Sci* 2013, **36**:181–204.

63. Sommer MA, Wurtz RH: **Influence of the thalamus on spatial visual processing in frontal cortex**. *Nature* 2006, **444**:374–377.

64. Eliades SJ, Wang X: **Neural substrates of vocalization feedback monitoring in primate auditory cortex**. *Nature* 2008, **453**:1102–1106.

65. Keller GB, Hahnloser RHR: **Neural processing of auditory feedback during vocal practice in a songbird**. *Nature* 2009, **457**:187–190.

66. Egner T, Monti JM, Summerfield C: **Expectation and Surprise Determine Neural Population Responses in the Ventral Visual Stream**. *J Neurosci* 2010, **30**:16601–16608.

67. Schneider DM, Nelson A, Mooney R: **A synaptic and circuit basis for corollary discharge in the auditory cortex**. *Nature* 2014, **513**:189–194.

68. Keller GB, Bonhoeffer T, Hübener M: **Sensorimotor mismatch signals in primary visual cortex of the behaving mouse**. *Neuron* 2012, **74**:809–815.

69. Zmarz P, Keller GB: **Mismatch Receptive Fields in Mouse Visual Cortex**. *Neuron* 2016, **92**:766–772.

70. Attinger A, Wang B, Keller GB: **Visuomotor Coupling Shapes the Functional Development of Mouse Visual Cortex**. *Cell* 2017, **169**:1291–1302.e14.

** This study shows that mismatch signals in V1 – responses to deviations of actual from expected visual feedback during locomotion – are dependent on experience and do not develop if mice are reared with random optic flow feedback during locomotion. Further results indicate that these mismatch signals are driven by an excitatory efference copy signal and a transient release from inhibition mediated by somatostatin-positive interneurons.

71. Saalmann YB, Kastner S: **Cognitive and perceptual functions of the visual thalamus**. *Neuron* 2011, **71**:209–223.

72. Kanai R, Komura Y, Shipp S, Friston K: **Cerebral hierarchies: predictive processing, precision and the pulvinar**. *Philos Trans R Soc B Biol Sci* 2015, **370**.

73. Gavornik JP, Bear MF: **Learned spatiotemporal sequence recognition and prediction in primary visual cortex**. *Nat Neurosci* 2014, **17**:732–737.

74. Kok P, Brouwer GJ, van Gerven MAJ, de Lange FP: **Prior expectations bias sensory representations in visual cortex**. *J Neurosci Off J Soc Neurosci* 2013, **33**:16275–16284.

75. Petro LS, Vizioli L, Muckli L: **Contributions of cortical feedback to sensory processing in primary visual cortex**. *Front Psychol* 2014, **5**.

76. Houde JF, Chang EF: **The cortical computations underlying feedback control in vocal production**. *Curr Opin Neurobiol* 2015, **33**:174–181.

77. Itokazu T, Hasegawa M, Kimura R, Osaki H, Albrecht U-R, Sohya K, Chakrabarti S, Itoh H, Ito T, Sato TK, et al.: **Streamlined sensory motor communication through cortical reciprocal connectivity in a visually guided eye movement task**. *Nat Commun* 2018, **9**:338.

78. Bruce CJ, Goldberg ME: **Primate frontal eye fields. I. Single neurons discharging before saccades**. *JNeurophysiol* 1985, **53**:603–635.

79. Ibrahim LA, Mesik L, Ji X-Y, Fang Q, Li H-F, Li Y-T, Zingg B, Zhang LI, Tao HW: **Cross-Modality Sharpening of Visual Cortical Processing through Layer-1-Mediated Inhibition and Disinhibition**. *Neuron* 2016, **89**:1031–1045.

80. Constantinople CM, Bruno RM: **Deep cortical layers are activated directly by thalamus**. *Science* 2013, **340**:1591–1594.

81. Mumford D: **On the computational architecture of the neocortex**. *Biol Cybern* 1992, **66**:241–251.

82. Bichot NP, Heard MT, DeGennaro EM, Desimone R: **A Source for Feature-Based Attention in the Prefrontal Cortex**. *Neuron* 2015, **88**:832–844.

83. Krauzlis RJ, Lovejoy LP, Zénon A: **Superior colliculus and visual spatial attention**. *Annu Rev Neurosci* 2013, **36**:165–182.

84. Wagner MJ, Kim TH, Savall J, Schnitzer MJ, Luo L: **Cerebellar granule cells encode the expectation of reward**. *Nature* 2017, **544**:96–100.

85. Wang L, Rangarajan KV, Gerfen CR, Krauzlis RJ: **Activation of Striatal Neurons Causes a Perceptual Decision Bias during Visual Change Detection in Mice**. *Neuron* 2018, **97**:1369–1381.e5.

86. Schmitt LI, Wimmer RD, Nakajima M, Happ M, Mofakham S, Halassa MM: **Thalamic amplification of cortical connectivity sustains attentional control**. *Nature* 2017, **545**:219–223.

87. Guo ZV, Inagaki HK, Daie K, Druckmann S, Gerfen CR, Svoboda K: **Maintenance of persistent activity in a frontal thalamocortical loop**. *Nature* 2017, **545**:181–186.

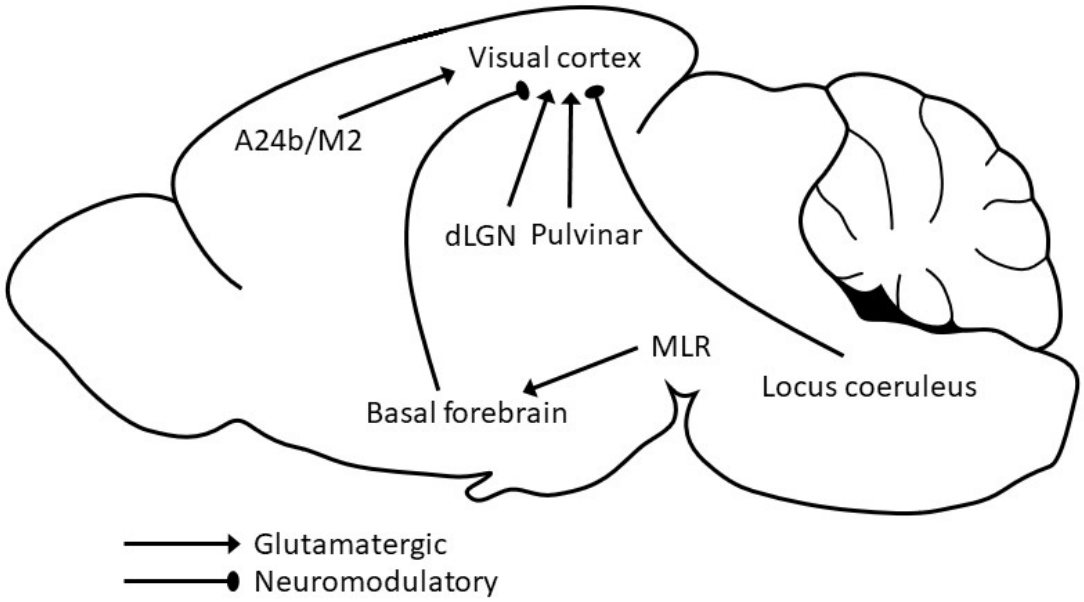

Figure 1

Schematic depicting the pathways conveying locomotion-related signals to V1. ACC/M2, anterior cingulate cortex and secondary motor cortex; dLGN, dorsolateral geniculate nucleus of the thalamus; MLR, mesencephalic locomotor region of the brainstem.

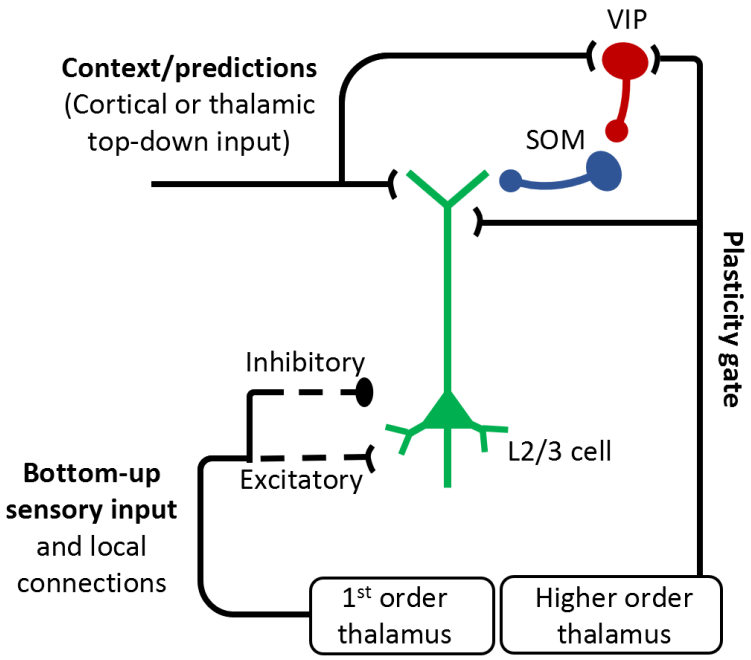

Figure 2

Schematic of a model in which input from higher-order thalamus gates plasticity in pyramidal neurons. Depolarization of pyramidal cell apical dendrites via this gating signal may enable either the association of top-down contextual and bottom-up sensory input, or allow potentiation of bottom-up or local connections. This potentially involves dendritic calcium spikes, facilitated by VIP-SOM interneuron-mediated disinhibition.

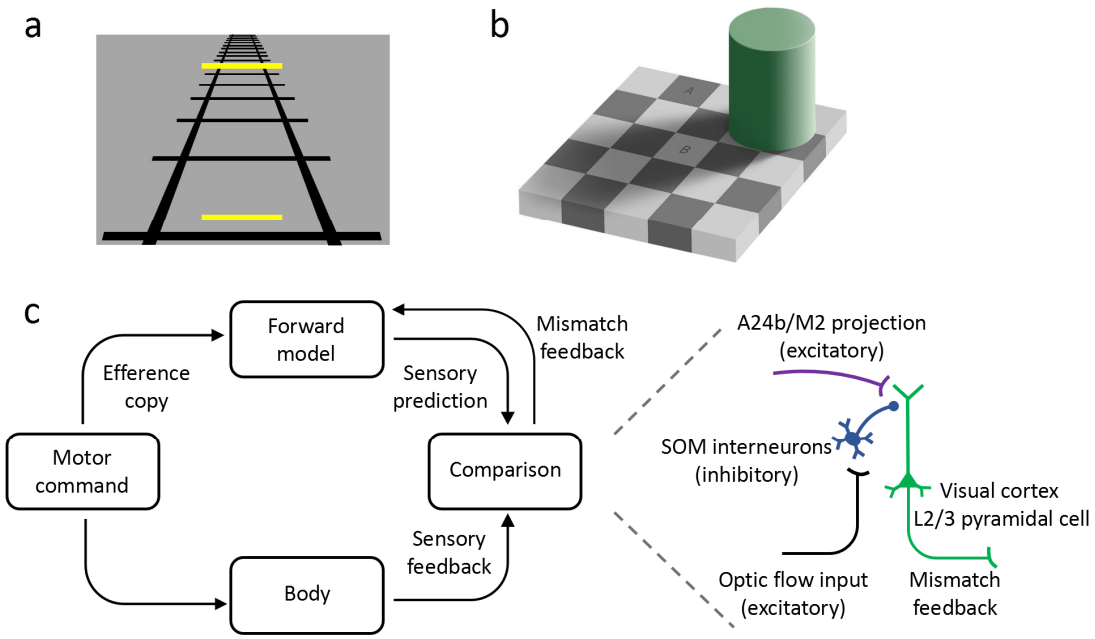

Figure 3

a, b) Visual illusions illustrating the powerful influence of expectation and internal models on visual perception. **a**) The yellow lines are the same length, but appear to be different, because of the image perspective and our expectation that objects that are further away appear smaller. **b**) The squares labeled A and B are of identical color and brightness, but appear different, because we take into account the darkening effect of the shadow when judging their brightness. **c**) Left, schematic depicting how internal models and predictions can inform sensori-motor processing. When a motor command is sent to the motor system , an efference copy of this command is used by a forward model to predict the sensory feedback that will result from the movement. This prediction and the true sensory input are compared, and if they do not match, a prediction error or mismatch signal can be fed back to the model to improve its predictions. Right, the circuit proposed by Keller and colleagues to compute a prediction error in layer 2/3 of V1, specifically for slower than expected or absent optic flow during locomotion. Top-down excitatory projections from ACC/M2 carry the running-related sensory predictions. Running-induced optical flow stimuli activate SOM interneurons which in turn inhibit L2/3 pyramidal cells, cancelling the excitation from the top-down predictions. If optical flow is absent during locomotion, SOM cell inhibition is removed evoking a mismatch response in a subset of pyramidal cells. Image in **b**), Wikimedia Commons.